UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,569	11/28/2000	John P. Anderson	015270-006446US	6102

20350 7590 07/08/2004

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
WALICKA, MALGORZATA A	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 07/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,569	ANDERSON ET AL.	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-131 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-131 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claim 1-30, 37-44 and 53, drawn to beta-secretase protein, classified in class 435, subclass 226.

II. Claim 31-36 and 45 drawn to crystalline composition comprising beta-sectretase and its inhibitor, classified in class 435, subclass 226.

III. Claim 45-52, drawn to beta secretase composition comprising beta secretase substrate, classified in class 435, subclass 226.

IV. Claim 54-55, drawn to antibodies against beta-secretase, classified in class 530, subclass 387.1.

V. Claim 56-77, drawn to nucleic acid encoding beta-secretase, expression vector, host cell and a recombinant method of production and purification beta-secretase using an affinity matrix, classified in class 435, subclass 226.3.

VI. Claim 78-85 and 104-107, drawn to a method of screening for compounds that inhibit Abeta production by inhibition of beta-secretase activity, the kit to be used in said method , classified in class 435, subclass 23.

VII. Claim 86-90, drawn to a method of screening for compounds that inhibit Abeta production using and inhibitor and a test compound that potentially binds beta-secretase and compounds selected by said method, classified in class 435, subclass 23.

VIII. Claim 91-103, and 118-120 drawn to beta-secretase inhibitors or their compositions to be used for the treatment of Alzheimer, classified in class 514, subclass 789.

IX. Claim 108-111, drawn to a knock-out mouse, classified in class 800, subclass 18.

X. Claim 112-113, drawn to a method of *in vivo* screening for drugs effective in the treatment of Alzheimer disease, classified in class 424, subclass 9.322.

XI. Claim 114-115, drawn to a method of treating of patient afflicted with Alzheimer disease by blocking hydrolysis of APP by using beta-secretase inhibitor, classified in class 424, subclass 9.2.

XII. Claim 116-117, drawn to a method of inhibiting proteolysis of APP to Abeta in a tissue classified in class 435, subclass 226.

XIII. Claim 121-126, drawn to method of diagnosing the presence of Alzheimer's disease in a patient by examining expression of beta-secretase, classified in class 435, subclass 6.

XIV. Claim 127-131, drawn to a method of purifying a beta-secretase protein using an affinity matrix which includes a beta secretase inhibitor, classified in class 435, subclass 226.

Claim 45 links inventions II and III and will be examined with the elected invention if invention II or III is elected.

Invention I-XIV are distinct each from the other for the following reasons.

Inventions I-V, VIII and IX are independent product having different chemical structure or chemical composition, as well as different functions. Because of recognized divergent subject matter and classification the inventions require separate search in the patent literature and publications.

Inventions of Group I and VI and VII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, invention of the product, which is beta-secretase may be used in materially different processes than method of screening for its inhibitors. For example, it may be used for production of antibodies.

Inventions of Group I and X, XI, XII and XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions, beta-secretase and methods X-XIII are not disclosed as capable of use together.

Inventions I and XIV are related as product made and process of making. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case beta-secretase protein can be purified by a

different method of protein purification, i.e., the one that does not use an affinity matrix comprising a beta-secretase inhibitor.

Inventions II and VI-VII as well as X-XIV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions, a crystal consisting of a beta secretase and its inhibitor is not disclosed as capable of use together whit any of methods VI-VII and X-XIV.

Invention III and VI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case invention of Group III, i.e., beta-secretase composition comprising beta secretase substrate can be used in another method of screening for beta-secretase inhibitor, for example in the method of Group VII.

Invention III and VII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different

process of using that product (MPEP § 806.05(h)). In the instant case invention of Group III, i.e., beta-secretase composition comprising beta secretase substrate can be used in another method of screening for beta-secretase inhibitor, for example in the method of Group VI.

Invention of Group III and X-XIV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the composition of Group III is not disclosed as capable of use in any of the methods X-XIV.

Inventions of Group IV and VI-VII and X-XIV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, antibodies of Group IV are not disclosed as capable of use in any of the methods VI-VII and X-XIV.

Inventions V and VI-VII and X-XII and XIV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, DNA molecule encoding beta-secretase is not disclosed as capable of use in any of methods of Group VI-VII and X-XII and XIV.

Invention V and XIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the DNA encoding different beta-secretase polypeptides may be used for their recombinant production and not for diagnosing the presence of or predilection for Alzheimer's disease.

Inventions VI-VII and X-XIV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, method of Groups VI-VII and X-XIV IV are all different having different steps and effects and are not disclosed as capable of use together.

Inventions VIII and X are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case beta-secretase inhibitors can be identified not in the vivo assay of group X, but an in vitro assay.

Inventions of Group VIII and XI-XII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the inhibitor of Group VIII can be used to inhibit beta-secretase *in vitro* and not *in vivo* as is the case for Group XI and XII.

Inventions VIII and XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, beta-secretase inhibitors cannot be used for examination of expression of beta-secretase in a patient. Therefor inventions are different.

Inventions VIII and XIV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the inhibitors of beta-secretase of group VIII can be used for the treatment of Alzheimer patients and not for the method of purification of beta-secretase.

Invention of Group IX, a knock-out mouse and inventions of Groups X-XIV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as

capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions none of the methods X-XIV can use the product that is the mouse with knock-out beta-secretase.

Inventions X-XIV are all unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, inventions X-XIV are all different methods having different steps and effects, and none of these methods is disclosed as capable of use with any other method.

Inventions of Group I-XIV are distinct for the reasons given above and have acquired a separate status in the art. Because of their recognized divergent subject matter and/or different classification, restriction for examination purposes as indicated is proper.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

In addition, if Group I is elected, Applicant is requested to elect beta-secretase species from the following group:

a) polypeptides having amino acid sequence starting with amino acid residue no.1 of SEQ ID NO: 2

b) polypeptides having amino acid sequence starting with amino acid residue no.22 of SEQ ID NO: 2

c) polypeptides having amino acid sequence starting with amino acid residue no.46 of SEQ ID NO: 2

d) polypeptide having amino acid sequence starting with amino acid residue no.58 of SEQ ID NO: 2

e) polypeptides having amino acid sequence starting with amino acid residue no.63 of SEQ ID NO: 2, and

f) mouse beta secretase of SEQ ID NO:65.

If Group II is elected, Applicant is requested to elect beta-secretase species from the following group:

a) polypeptides having amino acid sequence starting with amino acid residue no.1 of SEQ ID NO: 2

b) polypeptides having amino acid sequence starting with amino acid residue no.22 of SEQ ID NO: 2

c) polypeptides having amino acid sequence starting with amino acid residue no.46 of SEQ ID NO: 2

d) polypeptide having amino acid sequence starting with amino acid residue no.58 of SEQ ID NO: 2

e) polypeptides having amino acid sequence starting with amino acid residue no.63 of SEQ ID NO: 2, and

f) mouse beta secretase of SEQ ID NO:65.

If Group III is elected, Applicant is requested to elect a species from the group of substrates of SEQ ID NOs: 82-96.

If Group IV is elected, Applicant is requested to elect beta-secretase species from the following group:

a) polypeptides having amino acid sequence starting with amino acid residue no.1 of SEQ ID NO: 2

b) polypeptides having amino acid sequence starting with amino acid residue no.22 of SEQ ID NO: 2

c) polypeptides having amino acid sequence starting with amino acid residue no.46 of SEQ ID NO: 2

d) polypeptide having amino acid sequence starting with amino acid residue no.58 of SEQ ID NO: 2, and

e) polypeptides having amino acid sequence starting with amino acid residue no.63 of SEQ ID NO: 2.

If Group V is elected, Applicant is requested to elect DNA molecules encoding beta-secretase species from the following group:

a) polypeptides having amino acid sequence starting with amino acid residue no.1 of SEQ ID NO: 2

b) polypeptides having amino acid sequence starting with amino acid residue no. 22 of SEQ ID NO: 2

c) polypeptides having amino acid sequence starting with amino acid residue no. 46 of SEQ ID NO: 2

d) polypeptide having amino acid sequence starting with amino acid residue no. 58 of SEQ ID NO: 2,

e) polypeptides having amino acid sequence starting with amino acid residue no. 63 of SEQ ID NO: 2, and

h) mouse beta secretase of SEQ ID NO: 65.

If Group VII is elected, Applicant is requested to elect a species from the group of substrates of SEQ ID NOs: 82-96.

If Group VIII is elected, Applicant is requested to elect a species from the group of inhibitors of SEQ ID NOs: 72, 78, and 81.

If Group XIII is elected Applicant is requested to elect DNA molecules encoding beta-secretase species from the following group:

a)polypeptides having amino acid sequence starting with amino acid residue no.1 of SEQ ID NO:2

b) polypeptides having amino acid sequence starting with amino acid residue no. 22 of SEQ ID NO: 2

c) polypeptides having amino acid sequence starting with amino acid residue no. 46 of SEQ ID NO: 2

d) polypeptide having amino acid sequence starting with amino acid residue no. 58 of SEQ ID NO: 2, and

e) polypeptides having amino acid sequence starting with amino acid residue no.63 of SEQ ID NO: 2.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, 1-4, 18-23, 25-30, 31, 35-36, 47, 54-56, 61-100, 104-107, 112-122 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include

all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (571) 272-0944 and the right fax number is (571) 273-0944. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m. EST.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (571) 272-0928. The fax phone number for this Group is (571) 273-0937.

Malgorzata A. Walicka, Ph.D.
Art Unit 1652
Patent Examiner

RELEASED FOR ENTRY
PRIMARY EXAMINER
GROUP 1600
1600